Percutaneous Treatment of Thoracic Malignancy
A good portion of this lecture was adopted/modified from lectures given by William Moore, MD to this Physics 210 class from previous years.

**Credentials**

**Positions**
NYU Langone Medical Center  
Member of the Faculty, Department of Radiology  
Clinical Director, Radiology Information Technology  
Thoracic Imaging

**Board Certifications**
American Board of Radiology - Diagnostic Radiology, 2015

**Education and Training**
Fellowship, NYU School of Medicine, Thoracic Radiology, 2004  
Residency, Stony Brook University Medical Center, Diagnostic Radiology, 2004  
MD from Albany Medical College, 1999
Objectives

• Epidemiology of Lung Cancer.
• Technique of Percutaneous Ablation.
• Radiofrequency Biology of Cell Death.
• Cryobiology of Cell Death.
• Imaging Follow–up.
• Preliminary Data.
Epidemiology of lung cancer.

• Lung cancer is the leading cause of cancer related death for both men and women in the United States.

• In 2009:
  – estimated 219,440 cases of lung cancer diagnosed in the US and 1.3 million cases worldwide.
  – 159,000 deaths from lung cancer were estimated in the United States in 2009
Risk factors for Lung Cancer

- Cigarette smoking is by far the most important risk factor for lung cancer; risk increases with both quantity and duration of smoking.

- Cigar and pipe smoking also increase risk.

- Exposure to radon gas released from soil and building materials is estimated to be the second leading cause of lung cancer in Europe and North America.

- Other risk factors include occupational or environmental exposure to secondhand smoke, asbestos (particularly among smokers), certain metals (chromium, cadmium, arsenic), some organic chemicals, radiation, air pollution, diesel exhaust, and paint.

- Risk is also probably increased among people with a medical history of tuberculosis.

- Genetic susceptibility plays a contributing role in the development of lung cancer, especially in those who develop the disease at a young age.
Radon is a radioactive gas that when airborne can be inhaled into the lungs where it decays by alpha emission.
Cancer Deaths 1930 - 2013

- Cancer deaths are generally on the decline since the early 1990s.
- Why the spike in lung/bronchus related deaths?
- What happened in the late 1930s for men? Late 1960s for women?
- Why the sharp decline in lung/bronchus related deaths after the early 1990’s for men and leveling off for women?
Cancer Deaths 1930 - 2013

<table>
<thead>
<tr>
<th>Estimated Number* of New Cancer Cases and Deaths by Sex, US, 2013</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
</tr>
<tr>
<td><strong>All Sites</strong></td>
</tr>
<tr>
<td>Both Sexes</td>
</tr>
<tr>
<td>------------</td>
</tr>
<tr>
<td>1,600,290</td>
</tr>
<tr>
<td><strong>Oesophagus</strong></td>
</tr>
<tr>
<td>Both Sexes</td>
</tr>
<tr>
<td>190,420</td>
</tr>
<tr>
<td><strong>Colon</strong></td>
</tr>
<tr>
<td>Both Sexes</td>
</tr>
<tr>
<td>190,420</td>
</tr>
<tr>
<td><strong>Bladder</strong></td>
</tr>
<tr>
<td>Both Sexes</td>
</tr>
<tr>
<td>190,420</td>
</tr>
<tr>
<td><strong>Skin (excluding basal and squamous)</strong></td>
</tr>
<tr>
<td>Both Sexes</td>
</tr>
<tr>
<td>190,420</td>
</tr>
<tr>
<td><strong>Uterus</strong></td>
</tr>
<tr>
<td>Both Sexes</td>
</tr>
<tr>
<td>190,420</td>
</tr>
<tr>
<td><strong>Lymphomas</strong></td>
</tr>
<tr>
<td>Both Sexes</td>
</tr>
<tr>
<td>190,420</td>
</tr>
<tr>
<td><strong>Leukemias</strong></td>
</tr>
<tr>
<td>Both Sexes</td>
</tr>
<tr>
<td>190,420</td>
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</tbody>
</table>

*Rounded to the nearest 10 estimated new cases except basal and squamous cell skin cancers and in situ carcinomas except urinary bladder. About 64,640 cases in situ of the female breast and 63,300 melanomas in situ will be newly diagnosed in 2013. Estimated deaths for colon and rectal cancers are combined. More deaths than cases may reflect lack of specificity in recording underlying cause of death in death certificates and/or are not included in the case estimates.

Source: Estimated new cases are based on cancer incidence rates from 40 states and the District of Columbia during 2000-2003 as reported by the North American Association of Central Cancer Registries (NAACCR), representing about 14% of the US population. Estimated deaths are based on US mortality data during 1999-2009.

National Center for Health Statistics, Centers for Disease Control and Prevention.

Anatomy of the Lungs

http://anatomy-medicine.com/respiratory-system/57-the-lungs.html
Anatomical View of the Thoracic Cavity

- Trachea
- Heart
- Upper Lobe
- Middle Lobe
- Lower Lobe
- SVC
- Brachiocephalic veins
- Carotid Arties
- Pulmonary Artery
- Upper Lobe
- Ascending Aorta & Aortic Arch
- Lower Lobe
So how do we find a lung cancer?
So how do we find a lung cancer?

- Chest x-ray
- CT
So how do we find a lung cancer?

- Chest x-ray
- CT
- Bronchoscopy
- Findings metastatic disease elsewhere
Bronchoscopy

Bronchoscopy Procedure

Anatomy of the Bronchi/Lungs

Normal Main Right and Left Bronchi

Abnormal Bronchi
Standard Therapy for Lung Cancer:

- Lobectomy is the standard therapy for stage I non-small cell lung cancer (NSCLC).
- 5-year survivals as great as 80-90% and local recurrence rates of 5%.
- Unfortunately, only 30% of cases are resectable at the time of diagnosis.
Limited Resection:

• For the moderately compromised patient, sublobar resection is an option.
  – The main concern with sublobar resection is the increased local recurrence relative to lobectomy.
• For patients who are unable to tolerate pulmonary resection, external beam radiation (XRT) has traditionally been used.
External Beam Radiation:

• Treatment results are inferior to those of resection.
  – In a study of Stage 1 Lung cancers who received XRT of at least 60 Gy.
    • 3 year survival 19%.*
    • 5-year survivals 12%.*
  – Median survival is estimated at 19.9 months.**

** Chest: 2002;121;1155-1158
So what else could we do?
Local therapy has been tried

- What is the goal?
  - Cure
- What could we use?
  - Laser
  - Radionuclides
  - Radiofrequency
  - Freezing
  - Heating
General Ablation Technique:

- CT guidance is used for ALL lung applications
- We use general Anesthesia for all procedures.
  - Total anesthesia time is about 1-1.5 hours.
RFA technique:

- RFA Electrode
- RF Generator
- Patient return/grounding pads
RFA technique:
RITA/Angiodynamics

- Starburst Probes
  - We use the Starburst Talon 4 cm probe.
  - This has a flexible handle which is 20 cm long.
  - Perfect for CT applications.
- Sterile saline infusion pump system
  - Saline goes into the patient and diffuses among the lung propagating the RF signal (0.1 cc/min)
Cool-Tip Electrode
RFA technique:

Valley-labs

- The single probe:
  - This is for smaller lesions.
  - There is a 3 cm exposed tip.
Cluster tip probe.

– Three separate tips are on this single shaft probe. This has a 3 cm tip exposure. With a
Tumor Biology with RFA:

• At 45°C cellular swelling begins.
• The minimal acceptable tissue temperature for cell death is 60°C.
  – Cellular proteins are denatured
  – Enzymes are deactivated
  – Cellular death results.
Tumor Biology with RFA:

• At 105-115°C charring of tissue can occur.
  — Cavitation or gas formation also occur at this temperature.

• The impedance (tissue resistance to energy flow) increases dramatically.

• This is a problem in the lung because of possible air emboli to the brain.
• Stroke is a known risk with RFA.
Cryoablation

• This is a freezing procedure.
• Just like the RFA we place a needle into the lesion and rather then heat it up we freeze it.
### Isotherms form

**Right Angle CryoProbe**

<table>
<thead>
<tr>
<th>Temperature (°C)</th>
<th>Diameter (MM)</th>
<th>Length (MM)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0°C</td>
<td>37</td>
<td>56</td>
</tr>
<tr>
<td>-20°C</td>
<td>24</td>
<td>44</td>
</tr>
<tr>
<td>-40°C</td>
<td>16</td>
<td>36</td>
</tr>
</tbody>
</table>
PCT Technique:

- Depends on the size of the lesion.

• Small lesions (1-2 cm) - Single Needle; place the needle in the center of the lesion.
PCT Technique:

- Larger Lesions (>2.0-3.5 cm)
- Cluster technique
  - Several needles clustered around the lesion.
Ablation Protocol

• We perform a freeze-thaw-freeze cycle on all tumors.
  • 10 minute freeze
    – (-140°C)
  • 8 minute thaw
    – (Never go above 0°C)
  • 10 minute freeze
  • 3 minute thaw to remove the needle from the ice block.

Total Ablation time 28 minutes
1996
Argon Based
Joule-Thompson Cryoprobes

To freeze

To warm
Different gases have different Joule–Thomson (Kelvin) coefficient. Helium is warmer at 1 atmosphere while most other gases like Argon get colder.

We use the argon through the orifice to freeze and the helium to warm.
The cryotube is cooled by rapid expansion of a cooled gas through a narrow opening.
Cryobiology

Mechanisms of Cell Destruction
Freezing Damage Mechanisms

Freezing tissue damages cells in two ways:

1. Direct damage (to the cells) at the time of cryoablation
   - Slow cooling injury
   - Fast cooling injury

2. Indirect damage (to the tissue) following cryoablation
   - Ischemia - an inadequate blood supply to an organ or part of the body.
   - Apoptosis - process of programmed cell death that occurs in multicellular organisms
Direct Damage

When cells are frozen quickly:

– Water is trapped inside the cell because of how fast the temperature decreases.
– This results in Intracellular Ice Formation (IIF).
– The cytoplasm becomes supercooled.
– This damages the cell membrane.
– Holding the freeze causes recrystallization increasing cell damage.
Direct Damage

When cells are frozen slowly:

– Ice forms in the extracellular matrix
– The cell dehydrates but now has more concentrated cytoplasm
– Upon thawing cell rehydrates and expands beyond the membrane resulting in lysis or the breakdown of the cell membrane
Indirect Damage

• Two theories
  – Blood vessel engorgement
    • Ice formation causes vessel wall engorgement and distention resulting in stasis or blood reduced flow.
  – Damage to the endothelial cells
    • Almost all tissues depend on a blood supply, and the blood supply depends on endothelial cells, which form the linings of the blood vessels.
    • Endothelial cells have a remarkable capacity to adjust their number and arrangement to suit local requirements.
Indirect Damage

− Damage to the endothelial cells
  • They create an adaptable life-support system, extending by cell migration into almost every region of the body.
  • If it were not for endothelial cells extending and remodeling the network of blood vessels, tissue growth and repair would be impossible.
  • Cancerous tissue is as dependent on a blood supply as is normal tissue
  • It is hoped that by blocking/stopping the formation of new blood vessels, it may be possible to block the growth of tumors
  • Much like direct causes but this results in decreased blood flow to the tumor.

• Final result necrosis
Complications: for RFA and PCT
Immediate complications:

- **Pneumothorax** - a collapsed lung. A pneumothorax occurs when air leaks into the space between your lung and chest wall. This air pushes on the outside of your lung and makes it collapse. In most cases, only a portion of the lung collapses.

  - Small: 30% of cases performed
    Up to 50% in literature
  - Large: 20%; all required chest tubes
    - Three required prolonged hospitalization.

[Link to NLM Medline Plus](https://www.nlm.nih.gov/medlineplus/ency/presentations/100150_2.htm)
Immediate complications:

Pulmonary Hemorrhage: acute bleeding from the lung, especially in the upper respiratory tract and the trachea

Minor degrees in almost all cases.

Hemoptysis: the coughing up of blood.
Moderate (200 cc ~ 1/5 L) in 1 case.
Follow-up?

We follow patient with CT with contrast and Positron Emission Tomography (PET) imaging.
Contrast CT

• CT works by stopping the beam of radiation (x-rays) as it passes through a structure.
  – The radiation is collected by the detector and then depending on the density of the structure it will give a specific level of gray – Hounsfield Unit.

• When we add contrast (aka Iodine) structures that are vascular have more iodine in them
  – More iodine means more attenuation of x-ray beams.
  – Why would you want this?
PET

- Works by given a radioactive substance which emits a high energy particle;
  - The radioactive substance (Fluorine) is given to the patient which is coupled to FDG-a glucose analog.
  - This particle is radioactive and breaks down with time. $T_{1/2} \sim 3$ hrs.
  - We inject a standard amount 10-13 mCi and image 1 hour later.
PET

- The radioactive Fluorine decays and gamma rays are produced.
  - This means that the particle (positron) meets its antimatter counterpart (electron) and the two masses disappear and to conserve mass/energy two photons are produced and each photon goes in opposite direction.
  - 511 keV at 180 degrees to each other.
PET

- The detector will only image the particles that hit the detectors at the same time at 180 degrees.
- The glucose is held in metabolically active cells because of the fluoride which is added.
6 month SUV 1

12 month SUV 3.8
Standardized Uptake Values

SUV = Standardized Uptake Values

\[ SUV = \frac{r}{a'/w} \]

- Where \( r \) is the radioactive activity concentration [kBq/ml] measured by the PET scanner within a region of interest (ROI), \( a' \) is the decay-corrected amount of injected radiolabeled FDG [kBq], and \( w \) is the weight of the patient [g].

- The use of SUVs as a measurement of relative tissue/organ uptake facilitates comparisons between patients, and has been suggested as a basis for diagnosis.

- The greater the uptake value in a large lesion the greater the chance it’s a cancer.
Pre-treatment

1 year post-treatment
Survival after Cryoablation

Percent survival

Survival Time (Months)

75.1%
Conclusions:

• RFA and Cryoablation are safe alternatives to standard non-surgical therapy for lung cancer and pulmonary metastatic disease.
• Long term data in the lung is starting to surface for RFA but not PCT.
• Carefully, performed clinical trials are necessary to determine the exact role of these interventions in patients with lung cancer.
References: